An Introduction to 5-fluorouracil and its effects on *crithidia fasciculata*

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Fluorouracil

- medication used in chemotherapy
- works as a thymidylate synthase (TS) inhibitor, used to block synthesis of pyrimidine thymidine
- 5-FU causes a decrease in dTMP, which induces thymineless cell death
Fluorouracil

5-FLUOROURACIL

5,10-methylene tetrahydrofolate (cofactor)

Deoxyuridine → Thymidine → DNA synthesis

Neoplastic cell
Activation of 5-fU

- Capecitabine: an orally administered prodrug of 5-FU
- Capecitabine is converted by carboxyl esterase (liver) to 5-DFCR and then to 5-DFUR by cytidine deaminase
- Cytidine deaminase expressed in both liver and tumor
- 5-DFUR converted to 5-FU by thymidine phosphorylase
tumor specificity: because thymidine phosphorylase is expressed in a high level in malignant tumors relative to normal tissue
Fluorouracil: common usage

Colon and rectal cancer
  Anal cancer
  Breast cancer
Gastrointestinal cancers including: anal, esophageal, pancreas and gastric cancer
  Head and neck cancer
  Unknown primary (squamous cell)
  Neuroendocrine tumors
    Thymic cancers
    Cervical cancer
    Bladder cancer
    Hepatobiliary cancers
Adverse effects

- Nausea
- Vomiting
- Diarrhea
- Headache
- Alopecia (hair loss)
- Photosensitivity
- Itch
- Cardiotoxicity
- Persistent hiccups
- Mood disorders (irritability, anxiety, depression)
Crithidia fasciculata

- Trypanosome parasite
- Infects mosquitos
- Related to the parasites *Trypanosoma brucei gambiense* and *Trypanosoma cruzi*, which cause African Sleeping Sickness and Chagas’ disease.
Fluorine NMR

- Utilizes nuclear magnetic resonance (NMR) to identify $^{19}\text{F}$

- Real time FNMR used to measure the presence of the drug (5-fluorouracil) in the supernatant of the cells over time

- Height of the peaks indicate relative concentration
Fluorouracil on *Crithidia fasciculata*

- **Hypothesis:** Fluorouracil will affect the growth rate of parasite

- **Treatment:** *Crithidia fasciculata* + different fluorouracil concentration

- **Experiment:** *Crithidia fasciculata* were incubated in 5-FU in DMSO solution (5mmol, 1mmol, 0.2mmol, 0.04mmol, 0.008mmol or 0.0016mmol). Data were collected from OD600 growth curve

- **Result:** the growth rate of *Crithidia fasciculata* in 5-FU in DMSO solution with different concentration showed no significant difference

- **Conclusion:** 5-FU does not show an effect on *Crithidia fasciculata*
References

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